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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,965	03/31/2004	Robert Falotico	CRD-5073 NP	7706

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
03/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/813,965	FALOTICO ET AL.	
	Examiner	Art Unit	
	JENNIFER M. KIM	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 16, 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,9 and 10* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed December 16, 2009 have been received and entered into the application.

Response to Arguments

Applicants' arguments filed December 16, 2009 have been fully considered but they are not persuasive. Applicants argue that the combination of references (Sehgal and Rubino) fails to suggest the water solution of the specific concentrations claimed in independent claim1. Further, the Sehgal disclose that the composition is diluted with water shortly before administration via injection, therefore, this is not a stable solution containing water. This is not persuasive because Sehgal teaches that the composition preferably be diluted prior to administration does not mean it is unstable. Sehgal do not suggest that his composition is not stable and it is not an admission, but rather that dilution prior to administration is needed and it is the preference for their (unspecified/specified) need. Further, Rubino et al. teaches that the precipitation of rapamycin, particularly 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methyl-propionic acid (CCI-779) CCI-779 in a parenteral formulation can be prevented by use of the surfactant including vitamin E tocopherol propylene glycol succinate. There is a reasonable expectation of successfully formulating a stable injectable formulation

comprising rapamycin together with TPGS because Sehgal teach that various surfactants can be employed in rapamycin formulation and vitamin E-TPGS prevents precipitation of parenteral rapamycin formulation. One would have been motivated to combine these references and make such modification because they are drawn to same technical fields (constituted with same active ingredient and well known surfactant (e.g. vitamin E TGPS)), and pertinent to the problem which applicant concerns about (precipitation of rapamycin). MPEP 2141.01(a). Applicants argue that the amendment of claim 1 comes from Table 9. The specification and the table 9 have been carefully reviewed and considered but it is not persuasive. The limitations of about 1.7% by weight of ethanol, 4.3% by weight of vitamin E TPGS in water in an amount of about 92% by weight lack of literal support in the specification and Table 9 as originally filed. Therefore, Applicants' did not have possession of the claimed specific amounts of each of the active ingredients and therefore, it is a New Matter. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Applicant's amendment additional rejection presented in this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitations of about 1.7% by weight of ethanol, 4.3% by weight of vitamin E TPGS in water in an amount of about 92% by weight lack of literal support in the specification as originally filed. Therefore, Applicants' did not have possession of the claimed specific amounts of each of the active ingredients. This is a New Matter Rejection.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sehgal (EP 0041795 A2) of record in view of Rubino et al. (US2004/0167152 A1) of record.

Sehgal teaches an injectable composition of rapamycin, suitable for intravenous administration comprising about 1 to 20mg/ml of rapamycin composition and nonionic surfactants. (page 19, claim 1). This concentration range encompasses Applicants' range set forth in claim 1. Sehgal teaches that the rapamycin composition is prepared by dissolving rapamycin in an organic solvent which is capable of dissolving rapamycin and is miscible with the nonionic surfactant such as ethanol, and adding the nonionic surfactant, if required, removing some or all of the organic solvent, and **adding water**. (page 6, line 4- page 7, line 5). Sehgal illustrates the preparation of an injectable rapamycin composition by removing ethanol by evaporation. (page 8, example 1, claim 7). Sehgal teaches that various surfactant can be employed in the composition. (page 3, claim 9).

Sehgal do not teach the amount of ethanol and vitamin E TPGS set forth in claim 1.

Rubino et al. teaches that the precipitation of rapamycin, particularly 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methyl-propionic acid (CCI-779) CCI-779 in a parenteral formulation can be prevented by use of the surfactant including vitamin E tocopherol propylene glycol succinate (Vitamin E TGPS). ([0021], abstract). Rubino et al. also teach that parenteral CCI-779 formulations can be formulated with the various concentrations of 0.05mg/ml, from 2.5mg/ml, from 5mg/ml, from 10mg/ml or from 25mg/ml up to approximately 50mg/ml. Rubino et al. teaches formulation comprising CCI-779 with water for injection sufficient quantity up to 100% (see examples).

It would have been obvious to one of ordinary skill in the art to incorporate vitamin E TPGS in Sehgal's parenteral rapamycin formulation because Sehgal teaches that various surfactants can be added in the formulation and because Rubino et al. teach that TPGS can prevent the precipitation of CCI-779 in a parenteral CCI-779 formulation. One would have been motivated to make such modification in order to avoid the precipitation of parenteral rapamycin formulation taught by Sehgal et al. by adding surfactant such as TPGS taught by Rubino et al. There is a reasonable expectation of successfully formulating rapamycin together with TPGS because Sehgal teach that various surfactants can be employed in rapamycin formulation and vitamin E-TPGS prevents precipitation of parenteral rapamycin formulation. With regard to the claimed residual content of residual ethanol content of 0.5% to less than 2%, such is obvious because Sehgal illustrates removing ethanol by evaporation upon the dissolution of rapamycin in the process of preparing the injectable formulation of rapamycin. Sehgal teaches that some or all of the ethanol content can be removed once the dissolution of rapamycin takes place. Therefore, the residual ethanol content of less than 2% is encompassed and obvious over the evaporation step involving removal of **some** of ethanol taught by Sehgal et al.

Furthermore, no unobviousness is seen in the optimum amounts of the active ingredients claimed because once the ingredients is known for stabilizing a pharmaceutical active agents and they are compatible with the active agent in a pharmaceutical composition, it is within the skill of the artisan to determine the optimum amounts.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JENNIFER M KIM/
Primary Examiner, Art Unit 1617

Jmk
March 16, 2010